

REMARKS/ARGUMENTS

The Status of the Claims.

Claims 31, 33 to 35, 37 to 39, 41 to 47 are pending with entry of this amendment. Claims 1 to 32 being cancelled herein due to a restriction requirement made final; and 32, 36, and 40, being previously cancelled. Claims 33 and 45 to 47 are amended herein. These amendments introduce no new matter and support is replete throughout the specification. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with any objection or rejection of record.

With respect to claim 33, the amendment merely further focuses the identity of translated proteins to 95%, as described at paragraph 170 of the specification.

With respect to claim 45, support for the particular O-tRNA and O-RS can be found throughout the specification. For example, see specification at paragraphs 56 to 88, the Sequence Listing, the Figures, and Examples.

With respect to claim 46, the amendment merely deletes an aspect without addition of subject matter.

With respect to claim 47, the support for the aminoacetylation with one of two redox active amino acids can be found throughout the specification. For example, see specification at paragraph 89.

Applicants submit that no new matter has been added to the application by way of the above Amendment. Accordingly, entry of the Amendment is respectfully requested.

The Election/Restriction Requirement.

Pursuant to a restriction requirement made final, Applicants cancel claims 1 to 31 with entry of this amendment. Please note, however, that Applicants reserve the right to file subsequent applications claiming the canceled subject matter and the claim cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action.

35 U.S.C. §112, Second Paragraph.

Claim 33 was rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite because of the term "at least 75% identical to that of a wild type". To the extent that the amended claim is deemed indefinite, Applicants traverse.

Proteins of the invention include, e.g., two or more unnatural redox amino acids in their sequence. Therefore, the proteins of the invention are not typically expected to be 100% identical to proteins from which they may be derived. Applicants respectfully posit that the current amendment further limiting proteins to 95% identity provides, e.g., redox modified proteins with a reasonable likelihood of retaining functionality and utility. Such proteins would be further limiting over independent claim 31 at least with regard to, e.g., the nature of protein comprising the redox amino acids.

Because the amended claim is reasonably definite, Applicants respectfully request withdrawal of the rejection of claim 33.

35 U.S.C. §112, First Paragraph.

Claims 45 to 47 were rejected under 35 U.S.C. §112, first paragraph, for alleged failure to meet the written description requirement. To the extent that the currently amended claims are deemed to fail the written description requirement, Applicants traverse.

Current claims 45 to 47 are amended to provide functionally oriented structures. These structures are supported by original written descriptions. For example, the claims are limited to the listed redox active amino acids of independent claim 31; the O-RS structures described in the Orthogonal Aminoacyl-tRNA Synthetase and Source and Host Organisms sections; and, the O-tRNA structures described in the Orthogonal tRNA section of the original specification.

Because the amended claims are structurally and functionally described in the original specification, Applicants respectfully request withdrawal of claims 45 to 47.

35 U.S.C. §103(a).

Claims 31, 33 to 36, 38, 39 and 41 to 44 were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Schultz et al., (U.S. 7,045,337). Applicants traverse. Applicants note that claim 36 has been previously cancelled.

A proper analysis under the recently reaffirmed *Graham v John Deere* standard demonstrates the non-obviousness of the invention. As recently reaffirmed by the Supreme Court in *KSR International Co v. Teleflex* (550 U.S. ____ (2007); 127 S. Ct. 1727, 1740-41, 82 USPQ2d 1385-1396 (US 2007)), the appropriate standard for analyzing questions of obviousness is that:

the scope and content of the prior art are determined, differences between the prior art and the claims at issue are analyzed and the level of ordinary skill in the pertinent art is resolved. Against this background the obviousness or non-obviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unresolved needs, failure of others, etc. might be utilized to give light to the circumstances surrounding the origin of the subject matter to be patented.

Id. quoting *Graham v. John Deere of Kansas City* 383 U.S. 1, 17-18.

In addition, the Office has acknowledged that the “teaching-suggestion-motivation (TSM) test was *not* overturned by *KSR*.” Well established case law, such as described in MPEP 2143.01, still applies. For example, where the cited references teach away from the invention, it is not obvious. To show obviousness, the combination of cited references must teach all of the elements of the claims, the Office must provide a clear and articulated reason prompting one of ordinary skill in the art to make the proposed specific combination, and there must exist in the art a reasonable expectation of success in any proposed combination. Here, the rejection fails each of these requirements, as applied to the *Graham* factors.

Rejected independent claim 31 is as follows:

31. A composition comprising a protein, wherein the protein comprises two or more redox active amino acids selected from the group consisting of: a 3,4-dihydroxy-L-phenylalanine (DHP), a 3,4,5-trihydroxy-L-phenylalanine, a 3-nitro-tyrosine, a 4-nitro-phenylalanine, and a 3-thiol-tyrosine.

The rejection in the present Action at page 5 argues that Schultz '337 teaches "a specific ORS that preferentially aminoacylates an O-tRNA with a specific unnatural amino acid [not redox-active] which is incorporated into a protein", and "compositions comprising a protein, wherein the protein comprises at least two unnatural amino acids". At least one unnatural redox amino acid is listed in the reference. Based on these teachings, the

Action argues "it would have been obvious for a person of ordinary skill in the art to incorporate one, two or more unnatural amino acids including any type of redox-active unnatural amino acids such as those disclosed" in '337.

However, these allegations fail to state a *prima facie* case, do not allege a teaching of all limitations of the claim, and would not render the present claims obvious to one of skill in the art.

The law is clear and well established that there must be a statement of facts showing one of skill would be prompted to combine teachings in order for an untaught limitation to be considered obvious. An obviousness rejection requiring one of skill in the art to fill in missing aspects can not stand without a reasoned statement, based on cited facts, e.g., that one of skill would have had a reason to provide the missing aspect. "The fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish *prima facie* obviousness", MPEP 2143.01. A statement that modifications of the prior art to meet the claimed invention would have been well within the ordinary skill of the art at the time the claimed invention was made because ...all aspects of the claimed invention were individually known is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. See *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). Further, in *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000) the Court reversed obviousness rejections involving a technologically simple concept because there was no finding as to the principle or specific understanding within the knowledge of a skilled artisan that would have motivated the skilled artisan to make the claimed invention.

The mere fact the teachings of a reference can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination, e.g., to solve a specific identifiable problem. For example, in *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990), claims were directed to an apparatus for producing an aerated cementitious composition by drawing air into the cementitious composition by driving the output pump at a capacity greater than the feed rate. The prior art reference taught that the feed means can be run at a variable speed, however the court found that this does not require that the output pump be run at the claimed speed so that air is drawn

into the mixing chamber and is entrained in the ingredients during operation. Although a prior art device "may be capable of being modified to run the way the apparatus is claimed, there must be a suggestion or motivation in the reference to do so." *Id.* at 1432. That is, just because a prior art reference provides the starting materials and tools, does not mean it teaches one of skill to produce a specific product.

The Office's own Guidelines (Federal Register 72: No. 195; October 10, 2007), published after the recent Supreme Court decision in *KSR International Co v. Teleflex*, require the Office in an obviousness rejection to provide a statement as to why one of skill would have combined known elements. Even where results may be predictable or obvious to try, the Guidelines require showing "a reason that would have prompted [one of skill to practice the specific invention]" or a "finding that at the time of the invention, there had been a recognized problem [requiring the specific solution found in the claim]." "A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art. Although common sense directs caution as to a patent application claiming as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the art to combine the elements as the new invention does." *KSR* at page 5; emphasis added. "Under the correct analysis, any need or problem known in the field and addressed by the patent can provide a reason for combining the elements in the manner claimed." *KSR* requires that a problem be identified. In *KSR*, the solution to the identified problem of selecting a gas pedal sensor was found obvious, but here no problem is identified in the prior art that would have prompted the present inventions.

There is no statement in the present Action suggesting why one of skill would have ventured to prepare a composition comprising a protein with two or more of the listed redox active amino acids of claim 31. The Action only provides the conclusory statement that "it would have been obvious for a person of ordinary skill in the art" to practice the unique specific claimed inventions. The Action does not explain why one of skill would have, e.g., chosen the particular redox-active amino acids of claim 31, and decided for no apparent reason to, e.g., develop a new recombinant synthetase selected specifically to incorporate the specific redox-active amino acids into a protein, and specifically incorporate

redox amino acids two or more at a time. With diligent effort, Applicants find no problems in the cited art that would have prompted one of skill to attempt research specifically directed to produce a protein incorporating two or more redox-active amino acids.

On the other hand, the inventive Applicants had raised and addressed problems in research that led to the present inventions. For example, Applicants noted that proteins involved in redox reactions are limited to using, e.g., cysteine and/or a redox cofactor to catalyze redox reactions. Applicants have found that a solution to this problem could be to engineer proteins with two or more redox-active amino acids, e.g., with one redox-active amino acid substituted for a cysteine and a second redox amino acid substituted for a redox cofactor. The present invention is not the result of blind undirected efforts, but the diligent efforts directed to solve specific problems not enunciated in the prior art.

With regard to the cited Rodriguez reference, Applicants fail to see the relevance, except that he teaches away from the present invention with the single C-terminal substitutions.

Because the teachings of Schultz '337 and Rodriguez would not have prompted one of ordinary skill to produce a composition of a protein with two or more redox-active amino acids, the present claims can not be considered obvious. Dependent claims are not obvious at least because the associated independent claim 31 is not obvious. Moreover, with regard to dependent claims 41 to 44, Applicants believe that the cited art does not inherently teach the inventions. As discussed above, in citing *In re Miller*, just because a method is capable of adjustment to produce a specific product, does not make the product obvious. Further, according to extensive controlling case law (e.g., *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977); *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990); and, *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991)), for an aspect to be inherent in prior art, the aspect must necessarily (in all cases) be present in the art. Here, with regard to claim 42, for example, the proteins with single redox amino acids of the cited art are not necessarily capable of a shift in reduction potential requiring at least two redox active amino acids.

With regard to claim 44, redox catalysts are described in the present specification (if not physically reduced to practice), but are not inherent in the cited art. For

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Reply to Office Action of February 7, 2008

example, a protein of the prior art with a single redox amino acid would not necessarily be a redox catalyst protein.

Because the cited art does not teach all limitations of the claims, and the Action does not identify a reason one of ordinary skill in the art would have attempted to assemble the present specific compositions, the claims can not be considered obvious in light of Schultz '337 (or *KSR*). Applicants respectfully request withdrawal of the obviousness rejections.

CONCLUSION

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the claims are deemed not to be in condition for allowance after consideration of this Response, a telephone interview with the Examiner is hereby requested. Please telephone the undersigned at (510) 769-3510 to schedule an interview.

QUINE INTELLECTUAL PROPERTY LAW GROUP
P.O. BOX 458, Alameda, CA 94501
Tel: 510 769-3510
Fax: 510 337-7877
PTO Customer No.: 22798
Deposit Account No.: 50-0893

Respectfully submitted,

Gary Baker
Reg. No: 41,595

Attachments:

- 1) A transmittal sheet; and,
- 2) A receipt indication postcard.